CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH
SUMMARY OF TOXICOLOGY DATA

3-Iodo-2-Propynyl Butyl Carbamate

Chemical Code # 001938, Tolerance # 50237
SB 950 # 479

July 25, 1996
Revised: 9/4/02

I. DATA GAP STATUS

Combined, rat:	**No data gap, no adverse effect**
Subchronic, rat (oral):	**No data gap, no adverse effect**
(dermal):	**No data gap, no adverse effect**
Chronic toxicity, dog:	**Data gap, no study on file**
Oncogenicity, mouse:	**Data gap, inadequate study, possible adverse effect indicated**
Reproduction, rat:	**Data gap, inadequate study, no adverse effect indicated**
Teratology, rat:	**Data gap, inadequate study, no adverse effect indicated**
Teratology, rabbit:	**No data gap, no adverse effect**
Gene mutation:	**No data gap, no adverse effect**
Chromosome effects:	**No data gap, no adverse effect**
DNA damage:	**Data gap, inadequate study, no adverse effect**
Neurotoxicity:	**Not required at this time**

Toxicology one-liners are attached.

All record numbers through 117972 were examined.
**** indicates an acceptable study.**
Bold face indicates a possible adverse effect.
File name: T020904
Prepared by Green & Silva, 9/4/02
IPBC is an antimicrobial pesticide for non-food uses.
US EPA Reregistration Eligibility Document (RED) was published March, 1997.

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

These pages contain summaries only. Individual worksheets may contain additional effects.

COMBINED, RAT

**** 029, 030 114800, 114801, "3-Iodo-2-Propynyl Butyl Carbamate (IPBC) 104 Week Dietary Carcinogenicity Study in Rats", (Inveresk Research International, Musselburgh, Scotland, Everett, D.J., Perry, C.J., Hudson, P., Finn, J.P.; Report #: 5261 (March 18, 1988) and Mulhern, M., Everett, D.J., Perry, C.J., Hudson, P., Finn, J.P.; Report #: 7115 (March 21, 1989)). Troysan Polyphase P-100 (97% pure) was fed in diet to Sprague-Dawley rats (65/sex/dose) at 0, 20, 40 and 80 mg/kg/day for 104 weeks. At week 52, 15/sex/dose were necropsied (Report 5261) to assess chronic toxicity. At 104 weeks, 50/sex/dose were necropsied (Report 7115) to assess carcinogenicity. Chronic NOEL = 20 mg/kg/day (Group mean bodyweights for both the chronic and carcinogenicity studies were decreased at ≥ 40 mg/kg. Males at 80 mg/kg had hemoglobin, RBC counts and hematocrit that were statistically significantly decreased and at ≥ 40 mg/kg (chronic study) MCHC was decreased. Liver weights were increased at 52 weeks for both sexes at 80 mg/kg. Effects to the stomach were the primary macropathology effects observed at both 52 weeks (80 mg/kg) for chronic toxicity and at 104 weeks (≥ 40 mg/kg) for carcinogenicity. Histopathological effects were observed primarily in the stomach for both sexes at ≥ 40 mg/kg at 52 weeks and at 104 weeks and the incidence of effects had increased compared to 52 weeks. Salivary gland effects were observed in both sexes at ≥ 40 mg/kg (52 & 104 weeks).). No carcinogenicity. Possible adverse chronic effect: Treatment-related increase in stomach effect and effects to salivary glands at ≥ 40 mg/kg. M. Silva, 8/22/02.**

EPA NOEL < 20 mg/kg (Decreased male body weight gain.) Core minimum.

CHRONIC TOXICITY, RAT

Subchronic study:

50237 011 045437 "90-Day Subchronic Oral Toxicity Test in Rats. Test Material Troysan Polyphase," (Gordon, E.B., Yuster, J.; Bioassay Systems Corporation, Woburn, MA; BSC #: 11787; 5/11/84). Troysan Polyphase (98% pure) was administered by gavage to Sprague-Dawley rats (10/sex/dose) at 0 (corn oil), 20, 50 and 125 mg/kg, 5 days/week for 13 weeks. A satellite group received 125 mg/kg (10/sex, 5 days/week) for 13 weeks, then were held without treatment for 28 days after the 13 week treatment. NOEL = 20 mg/kg (Absolute and relative body weights were decreased in males at 125 mg/kg. Clinical signs (excess salivation, lethargic, wheezing, epistaxis) in males at ≥ 50 mg/kg and in females at 125 mg/kg. Both sexes at 125 mg/kg had increased chronic progressive nephrosis of kidney, liver cytomegaly (all animals at 125 mg/kg), forestomach irritation and cardiomyopathy.) This study is not acceptable. It is possibly upgradeable upon submission of clinical sign data (mentioned but not included), inclusion of all data mentioned in the results section in summary tables with statistical analysis. Possible adverse effects indicated (clinical signs, liver hyperplasia, cardiomyopathy) M. Silva, 8/2/02

EPA NOEL = 20 mg/kg (Increased liver weights.) Not acceptable to EPA.

008 037437 Duplicate of 011 045437

016 064012 Duplicate of 011 045437.

**** 028 114798 "91-Day Dermal Toxicity Study in Rats With Troysan Polyphase P-100," (Siglin, J.C.; Springborn Laboratories, Inc., Life Sciences Division, Spencerville, OH; SLS Study #: 3228.14; 12/6/91). Troysan Polyphase P-100 (97.5% pure) was dermally administered to Sprague-Dawley Crl:CD_BR VAF/Plus_ rats (10/sex/dose) at 0 (PEG 400 = vehicle), 50, 200 and 500 mg/kg/day (with occlusion) for 91 days (6 hours/day, 5 days/week). Systemic NOEL = 50 mg/kg (Male body weight gains were statistically significantly decreased ($p < 0.05$) at 500 mg/kg early in the study but thereafter weight gains were similar to controls. Cumulative body weight gains for males were statistically significantly decreased ($p < 0.05$) over days 1 – 29 at 500 mg/kg, but thereafter weights were similar to controls. For males, food consumption was intermittently statistically significantly decreased at $\geq$ 200 mg/kg. Dermal NOEL = 50 mg/kg (Clinical effects (erythema, edema, eschar, desquamation) and histopathology (acanthosis, exudate, hyperkeratosis, ulcer) on skin were observed at $\geq$ 200 mg/kg.).) Possible adverse effect to skin. Acceptable. Silva, 8/23/02**

EPA NOEL = 200 mg/kg. Core minimum.

CHRONIC TOXICITY, DOG

No study on file.

ONCOGENICITY, RAT

No study on file.

ONCOGENICITY, MOUSE

Dose-Rangefinding Study:

031 114802 "8 Week Dietary Dose Range Finding Study in Mice," (Atkinson, C., Perry, C.J., Aitken, R.; Inveresk Research International, Musselburgh, Scotland; IRI Project #: 436144; 11/26/87). Troysan Polyphase P 100 (3-iodo-2-propynyl butyl carbamate (IPBC), 97% purity) was fed in diet to CD- mice (10/sex/dose) at 0, 50, 250, 500 and 1000 mg/kg/day for 8 weeks. NOEL = 50 mg/kg/day (Decreased bodyweight gain and food consumption occurred in both sexes at $\geq$ 250 mg/kg/day (equivocal at 250 mg/kg). Increased absolute liver weights occurred in both sexes at $\geq$ 250 mg/kg/day. Gross pathology showed darkened livers at 250 mg/kg (males) and at $\geq$ 500 mg/kg (both sexes). Centrilobular hepatocyte enlargement with pigmentation occurred in both sexes at > 250 mg/kg. In all treated animals, there was evidence of redistribution and/or reduction of intracellular lipid in liver.) Not acceptable, since even numbered pages were not included in the report and since the study was not intended to be

performed according to FIFRA Guidelines. No adverse effects indicated. (Silva & Green, 8/26/02)

Definitive Study:

031 114803 "IPBC 78 Week Dietary Carcinogenicity Study in Mice", (Mulhern, M., Finn, J.P., Everett, D.J., Perry, C.J.; Inveresk Research International, Tranent, Scotland, Report # 7304, 6/16/89). Troysan Polyphase P 100 (3-iodo-2-propynyl butyl carbamate (IPBC), Batch P-2848-8603-P100; 97% pure) was fed in diet to CD-1 mice (50/sex/dose) at 0, 20, 50 and 150 mg/kg/day for 78 weeks. Plasma, RBC and Brain ChE were not inhibited. Systemic (chronic) NOEL < 20 mg/kg/day (Group mean bodyweights were slightly reduced for males (3-8%) and females (3-6%) at 150 mg/kg. Bodyweight gain was 23% (M) and 20% (F) lower at 150 mg/kg through week 78, compared to controls. Thyroids were enlarged macroscopically at 150 mg/kg in both sexes (especially males). There were histopathological thyroid effects in both sexes at all doses.) There was a statistically significant increase in hepatocytic adenomas at 150 mg/kg in males but not in females. The incidence of liver carcinomas in males was similar in all groups (3, 3, 3, 4 for control through high dose). Possible adverse effects indicated: Increased liver adenomas were reported at 150 mg/kg in males. Chronic (non-oncogenic) effects to thyroid also occurred. Currently this study is unacceptable, but is possibly upgradeable upon submission of FIFRA Guideline-recommended organ weights (liver, kidneys, brain, testes), along with a complete version of the dose range-finding study (Report # 5021 & IRI Project 335018). (Green & Silva, 8/27/02)

EPA NOEL < 20 mg/kg (Thyroid effects).

REPRODUCTION, RAT

032 114804 "Two Generation Oral (Dietary Administration) Reproduction Toxicity Study in the Rat (One Litter per Generation)", (Osterburg, I.; Reproduction Toxicology, Hazleton Laboratories Deutschland GmbH, Munster, West Germany; Report # 548-511/3, 10/16/87). Troysan Polyphase (3-iodo-2-propynyl butyl carbamate (IPBC), Batch #: 2710-8511-R100, purity not stated) was fed in diet to Sprague Dawley Crl:CD⁻ (SD) BR rats (25/sex/dose/generation) at 0, 120, 300 and 750 ppm for 2 generations (1 litter/generation) through weaning of F2 pups. Exposure began 14 weeks prior to mating of F0 parental animals. Parental NOEL = 120 ppm (During premating, both P and F1 parental food consumption was reduced intermittently in both sexes at 750 ppm. Body weight during premating was slightly decreased at ≥ 300 ppm in males. During gestation, P females had decreased body weight gain at 300 ppm but not at 750 ppm. Throughout premating, F1 parental males had decreased body weight and body weight gain at 750 ppm.) Reproductive NOEL = 300 ppm (Both F1 and F2 litter size and litter weights were decreased at 750 ppm. The F1 pups had decreased live birth index at 750 ppm. F2 pups had decreased live birth index at 750 ppm. There were no effects on reproductive parameters.) This study is not acceptable, since characterization of Troysan Polyphase (purity, stability, content) and analyses of dosing material (homogeneity, stability, concentration) were not included in the study. It is necessary to submit these data for a possible upgrade of this study to acceptable. No adverse effect. Green & Silva, 9/3/02.

EPA Parental NOEL = 300 ppm (Based on decreased parental body weights and food

consumption. Reproduction NOEL ≥ 750 ppm.

008 037438 "Preliminary Study for a 2 Generation Study in the Rat," (No author indicated; Hazleton Laboratories Deutschland GmbH; Project #: 511/1; no date). Troysan Polyphase (no characterization) was administered by gavage to 16 inseminated rats at 80 mg/kg. Data could not be interpreted, since there were no controls. Although most of the report was in German, there did not appear to be any treatment-related effects. (No worksheet). M. Silva.

TERATOLOGY, RAT

027 114797 "Final Report, Troysan Polyphase Oral (Gavage) Teratogenicity Study in the Rat," (Osterburg, I., Hazleton Laboratories Deutschland GmbH, Munster, West Germany, Report # 696-511/4, 12/86). Troysan Polyphase P100 (purity not stated) was administered by gavage to mated Sprague Dawley Crl:CD(SD)BR rats (28 – 38/dose) at 0 (corn oil), 20, 50 or 125 mg/kg/day on gestation days 6 through 15. Maternal NOEL = 20 mg/kg/day (Bodyweight gain was decreased and total litter resorptions was increased at ≥ 50 mg/kg.). Possible adverse effects indicated: Developmental NOEL = 20 mg/kg/day (Fetal malformations (cleft palate, bilateral anopthalmia) at 50 mg/kg and skeletal (scholiosis) and external malformations (mandible shortened, open eye) at 125 mg/kg were observed.). Not acceptable and probably not upgradeable (No dose justification, historical control data for total litter resorptions and fetal malformations, food consumption measurements, test article/dosing material characterization). At this time, the adverse fetal effects are considered to be treatment-related. Adverse fetal effects occurred at doses causing only mild maternal toxicity (transitional decreased body weight gain). (Green & Silva, 7/31/02).

EPA Maternal NOEL = 50 mg/kg (Decreased weight gain in dams.) Developmental NOEL = 50 mg/kg (Based on delayed ossification in fetuses.)

016 064015 Duplicate of 027 114797.

TERATOLOGY, RABBIT

Rangefinding Study:

035 117971, "Range-Finding Teratology Study in Rabbits with Troysan Polyphase P-100," (Siglin, J.C.; Springborn Laboratories, Inc. (SLS), Life Sciences Division, Spencerville, OH., Report # 3228.15; 8/17/92). Troysan Polyphase P-100 (97% 3-iodo-2-propynyl butyl carbamate) was administered by gavage to inseminated New Zealand White female rabbits (5/dose) at 0 (corn oil), 5, 15, 30, 50 and 80 mg/kg/day on gestation days 6 through 18. Maternal NOEL = 30 mg/kg/day (At 50 mg/kg, an increase in post-implantation loss and a decrease in mean number of viable fetuses was observed. Gross necropsy findings for 2/4 females found dead at 80 mg/kg showed gastrointestinal changes. However, tissue autolysis occurred to the point where gross necropsy could not be performed on the other 2/4 females at 80 mg/kg that had died on study. At 80 mg/kg females showed unkempt appearance, decreased activity, emaciation, dehydration, few feces, no feces and desquamation around the mouth. At 80 mg/kg bodyweight continued to decrease.) Developmental NOEL = 30 mg/kg/day (External

malformations occurred in 2/21 fetuses at 50 mg/kg (exencephaly, flexed paw) from 2 different litters). No adverse effects indicated. Data are supplemental. (H. Green & M. Silva, 3/8/02)

Definitive Study:

** 035 117972 "Teratology Study in Rabbits with Troysan Polyphase P-100," (Siglin, J.C.; Springborn Laboratories, Inc. (SLS), Life Sciences Division, 553 North Broadway, Spencerville, OH., Report # 3228.16; 8/17/92). Artifically inseminated New Zealand White female rabbits received Troysan Polyphase P-100 (97% 3-iodo-2-propynyl butyl carbamate) at 0 (corn oil), 2, 20, and 50 mg/kg/day by gavage on gestation days 6 through 18. **Maternal NOEL** = 20 mg/kg/day (2 females died and 1 was sacrificed moribund at 50 mg/kg/day. There was an increase in post-implantation loss and decrease in mean number of viable fetuses at 50 mg/kg. The number of live litters and the mean live litter size was reduced at 50 mg/kg/day. There was an increased incidence in few feces, no feces, soft stools, mucoid stools, brownish colored mucoid material in cage/tray, reddish colored material in cage/tray, fecal stain, various nose/mouth effects in dams at 50 mg/kg. Maternal food consumption at 50 mg/kg was reduced (18% to 40%) throughout treatment period. Group mean bodyweights were decreased by nearly 10% (day 19). There were statistically significantly decreased body weight gain throughout the study at 50 mg/kg.) **Developmental NOEL** = 20 mg/kg/day (There were increased fetal soft tissue and skeletal malformations at 50 mg/kg. There was an increased incidence in flexed paw, heart/great vessel anomaly, hydrocephaly and hyoid body/arch unossified at 50 mg/kg.) Acceptable. No adverse effect. (M. Silva & H. Green, 3/12/02).

EPA Developmental NOEL = 20 mg/kg; Developmental NOEL $\geq$ 50 mg/kg.

GENE MUTATION

010 045436, "Salmonella Typhimurium/Mammalian Microsome Plate Incorporation Assay with Compound IPBC", (N.E. McCarroll, Hazleton Laboratories America, Inc., Vienna, VA., Report # 2277-102, 7/24.84). Triplicate plates of *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537, and TA1538 were exposed in the presence and absence of activation (S9) to 3-iodo-2-propynyl butyl carbamate (IPBC) concentrations of 0 (untreated), 0 (DMSO), 0 (S9 fraction), 6.2, 18.5, 55.6, 166.7 and 500.0 _g/plate for 48 hours. A treatment-related increase in gene mutations was not observed. The positive controls functioned as expected. Currently this study is not acceptable but is possibly upgradeable with submission of the requested information (chemical characterization, dosing solution analyses/data for toxicity tests, individual plate counts). Green & Silva, 8/1/02

008 037441 Duplicate of 010 045436

016 064014 Duplicate of 010 045436

**** 026 114794, "Testing for Mutagenic Activity with Salmonella typhimurium TA 1535, TA 1537, TA 1538, TA 98, and TA 100," (C. G. Riach, Inveresk Research International Limited, Musselburgh, Scotland, Report # 4896, 6/20/89). *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537, and TA1538 were treated for 48 hours (3 plates/dose; with and without S9 metabolic activation) with Troysan Polyphase P-100 (98.68% 3-iodo-2-propynyl butyl carbamate) at 0 (DMSO), 1, 3, 10, 33, 100 and 333 Fg/plate (Test #1, +/- S9) or 0, 3, 10, 33, 100, 333 and 1000 Fg/plate (Test #2, + S9) or 1, 3, 10, 33, 100 and 333 Fg/plate (Test #2, no S9) and**

TA1535 treatment ranged from 3 to 1000 Fg/plate. An increased incidence in reverse mutations was not observed. Acceptable. (Green & Silva, 6/27/02).

CHROMOSOME EFFECTS

**** 026 114796, "Troysan Polyphase (IPBC): In Vivo Micronucleus Assay in Mice, Final Report," (N. McCarroll, Hazleton Biotechnologies Corporation, Vienna, VA., Report # 2277-103, 10/3/84). 3-Iodo-2-propynyl butyl carbamate (IPBC, 99% purity) was administered in a single dose by gavage to CD–-1 mice (15/sex/dose) at 0 (corn oil), 200, 660, and 2000 mg/kg. At 30, 48, and 72 hours after dosing, bone marrow was sampled (5/sex/dose). No increase in the frequency of micronucleated polychromatic erythrocytes was observed. Acceptable with no adverse effect. (Green & Silva, 7/29/02).**

008 037440 Duplicate of 026 114796

016 064013 Duplicate of 026 114796

DNA DAMAGE

026 114795 "Troysan Polyphase (IPBC): Assessment of Genotoxicity in an Unscheduled DNA Synthesis Assay Using Adult Rat Hepatocyte Primary Cultures," (D. McBride and C.G. Riach, Inveresk Research International, Mussel Burgh EH21 7UB Scotland, Report # IRI 737447, 1/21/88). Primary hepatocyte cell cultures obtained from Fischer 344 rats were treated (4 plates/dose) with IPBC (3-iodo-2-propynyl butyl carbamate) at 0 (DMSO), 3.0, 4.5, 6.0, 7.5, 9.0, 10.5, 12.0, and 13.5 _g/ml for 18 to 20 hours in a test for unscheduled DNA synthesis. Unscheduled DNA synthesis was not observed. Unacceptable and upgradeable (test article characterization, statistical analyses and clarification of grouping for individual data). (Green & Silva, 7/25/02).

NEUROTOXICITY

None submitted. The RED of US EPA, 1996, indicated that acute and subchronic neurotoxicity studies with cholinesterase were being required.

The following record numbers have been reviewed:

Record Number	Volume
037438	50237-008
037440	50237-008 (Duplicate to 114796).
037441	50237-008 (Duplicate to 045436).
045435	50237-010 (Duplicate to 114796).
045436	50237-010
064013	50237-016 (Duplicate to 114796).
064014	50237-016 (Duplicate to 045436).
064015	50237-016 (Duplicate to 114797).
114794	50237-026
114795	50237-026

114796	**50237-026**
114797	**50237-027**
114800	**50237-029**
114801	**50237-030**
114803	**50237-031**
114805	**50237-032**
114804	**50237-032**
117971	**50237-035**
117972	**50237-035**